Detection and Monitoring of Brain Injury After Cardiac Arrest

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Abstract—**Many of the resuscitated cardiac arrest patients are left with significant cerebral ischemia. The electroencephalograph (EEG) used in clinical neurophysiology can be utilized for the identification of cerebral injury. However, there is a compelling need to bring to the bedside state-of-the art instrument for rapid and accurate detection and monitoring of brain injury severity in cardiac arrest victims.**

The subband wavelet entropy and entropy rate are two quantitative measures for analyzing and segmenting the EEG signals. Markov process amplitude algorithm is also used to model the EEG signal to identify pathophysiological EEG changes. The above methods are based on an important observation related to the process of neurological recovery and the presence of spikes and bursts pattern manifested in the EEG. The EEG is measured from rodent brains in a controlled experimental brain injury model by hypoxic-ischemic cardiac arrest. Results show that wavelet entropy and Markov modeling are two techniques that can be used to segment the EEG and delineate the initial bursting periods in each subband.

Index Terms— **EEG, Brain Injury, Entropy, Wavelet Transform, Markov Modeling.**

I. Introduction

Cardiovascular disease (CA) is the major cause of death in UAE and the Arab Gulf Countries. According to statistics published in the United States, approximately one million CA survivors may develop a poor neurological outcome [1-4]. The recent technological advancements in defibrillators have resulted in a successful resuscitation of many patients. However, the majority of these surviving patients are left with significant neurological impairment [5-6], where the heart is functioning while the brain is damaged.

The EEG is a powerful tool for the identification of cerebral injury. Unfortunately however, its visual interpretation is subjective and prone to human errors due to eye scanning of long stretches of recordings. Therefore, there is a need to quantify the information content of the EEG. The Fourier Transform, the Wavelet Transform, chaos theory, and entropy are amongst many techniques which have been proposed to address this problem [7-11].

In a controlled experimental rodent brain injury model, an important observation is the presence of spikes and bursts pattern manifested in the EEG at various phases of brain injury [12-14]. At the early stages of recovery, it was noticed that the EEG signal is composed of a random spiking signal. The synchronization of a composite rhythm in the EEG may reflect the coherence in the phases of its spatial components. If the neural generators continue to fire in a synchronized manner, bursting is considered as a sign of a good neurological outcome. In case of severe brain injury, wherein the neural generators are desynchronized, the signal continues to be spiky and is associated with a bad neurological outcome. Although relative power of EEG signal may be useful in certain brain studies, it fails to reveal the order of bursting activity associated with recovery. To study the different statistical distributions associated with spiking and random background activity of EEG rhythms, we use quantitative measures related to the amount of "information" content of the signal. Subband Wavelet Entropy (SWE) is used to characterize the interactions between the bursting and random background of EEG rhythms [15]. The wavelet transform is useful for decomposing the EEG into multi-scaled components. For EEG signal sampled at 250 Hz, a five level decomposition results in the standard clinical bands of interest: Gamma (31.2–62.5Hz), Beta (15.6–31.2Hz), Alpha (7.8–15.6Hz), Theta (3.9–7.8Hz) and Delta (1.9-3.9Hz) [16].

Although entropy is a good measure of uncertainty, it is not possible to be neither interpreted nor standardized before and after injury. A reference entropy measure is needed. In real clinical applications, the entropy measure prior to brain injury is usually unavailable for most subjects or patients. One possible way to overcome this problem is by using the SWE and its rate of change. Before injury, the EEG signal is assumed to be stationary with entropy rate of change close to zero. However, during early recovery until the late recovery phases, the signal statistical characteristics are continuously changing and hence the entropy rate of change will not be equal to zero. Therefore, SWE rate of change is used to reflect the recovery process [17].

Signal modeling can also serve to quantify EEG data. Markov process amplitude algorithm is used to model the EEG signal to identify pathophysiological EEG changes during various phases of injury and recovery. The dynamics of the model coefficients is used to capture the presence of spiking and bursting in EEG [18-19].

The rest of the paper is organized as follows: In section II, various techniques used to quantify the EEG signal are described followed by some results in section III. Conclusions and suggestions for future work are included in section IV.

Manuscript received November, 14, 2006.

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II. METHODOLOGY

A. PROTOCOL

EEG signals were recorded from awake behaving rats after being subjected to controlled periods of asphyxia and cardiac arrest using the asphyxic cardiac arrest and resuscitation protocol as modified from Katz and colleagues [20]. Asphyxia was induced by stopping the ventilator and clamping the ventilator tubes for controlled time duration. Resuscitation was initiated by resuming mechanical ventilation at 100% O_2 at 90 breaths/minute and performing Cardio Pulmonary Resuscitation (CPR). After one hour of recovery, rats were extubated and allowed to breathe spontaneously. Two differential channels were recorded from the left and right fronto-parietal regions. The signals were lowpass filtered with 100Hz cut-off frequency prior sampling with 250 Hz. Fig. 1 shows the EEG signal recorded for a period of approximately 200 min. The EEG recording is divided in four parts: before asphyxia, baseline (BL), silence period (SP), early recovery (ER) and late recovery (LR).

Figs. 2 (a and b) show a 200 seconds period of an EEG signal recorded during the BL and ER periods respectively. It is noticed that the statistical characteristics of the EEG signal are different before and after injury.

B. Subband Wavelet Entropy and Entropy Rate of Change

The amount of information contained in a message is directly related to the uncertainty [21]. For a random variable, *X* with probabilities, $P(X = x_l)$, the average information per message emitted by the source (which could be the brain in our case) is called its entropy, denoted by *H(X)*. Hence,

$$H(X) = -\sum_l P(X = x_l)\log_2 P(X = x_l) \quad bits \qquad (1)$$

In the time-frequency domain, the EEG signal sampled at 250 Hz is divided into frames. Then, each frame is decomposed into the standard clinical bands of interest [15]. The wavelet coefficients sequence of the i^{th} frame EEG signal at resolution j is $\mathbf{d}^j = [d^j(1), d^j(2), \ldots\ldots, d^j(N)]$. The wavelet coefficients sequence $d_j(k)$ is used to compute the Subband Wavelet Entropy at scale j using:

$$H^j(i) = -\frac{\sum_k |d_j(k)|}{\sum_j \sum_k |d_j(k)|} \times \log_2 \left(\frac{\sum_k |d_j(k)|}{\sum_j \sum_k |d_j(k)|} \right) \qquad (2)$$

It is important to note that the entropy of the baseline EEG signal before injury is maximum. However, after injury, the statistics of the EEG signal change with different distributions of each frame of the recovering signal.

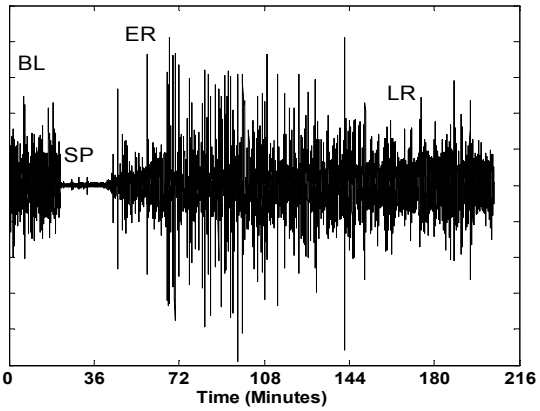
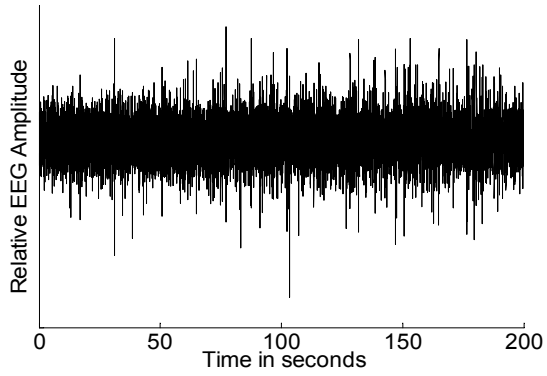
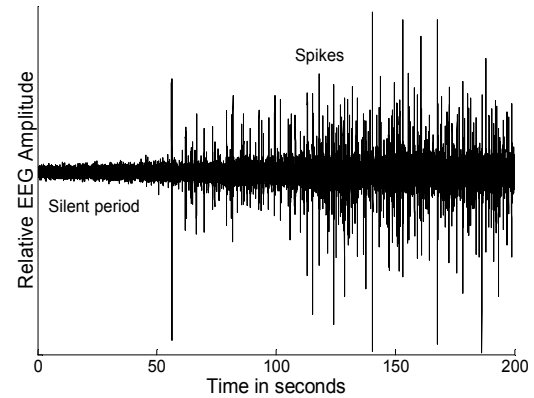


Fig. 1: Compressed EEG signal record. The recording is divided into Base line (BL), Silent period (SP) following arrest and resuscitation, Early recovery (ER), and Late recovery (LR) .



(a)



(b)

Fig.2: 200 seconds period of an EEG signal recorded (a) before and (b) after ischemia.

To reveal the dynamics of the SWE and avoid the need for baseline entropy, the entropy rate of change, $\dot{H}^j(i)$ is measured by [17]:

$$\dot{H}^j(i) = H^j(i) - H^j(i-1) \qquad (3)$$

If the statistical distributions of $\boldsymbol{d}^j_i$ and $\boldsymbol{d}^j_{i-1}$ sequences have similar characteristics then, $\left|\dot{H}^j(i)\right| \approx 0$. During BL, the spikes or bursts are absent and EEG signal is predominantly random, therefore we should expect low $\left|\dot{H}^j(i)\right|$. However, during the ER period, the spiking and bursting activity is strong and hence $\left|\dot{H}^j(i)\right| \neq 0$. With time, the random activity increases and the spikes merge forming bursts and finally the EEG signal is predominantly random. $\dot{H}^j(i)$ starts with relatively large value during the ER period, and decreases with time reflecting the EEG signal recovery. Hence, we conclude that if both $H^j(i)$ and $\dot{H}^j(i)$ are used then we will have a quantitative measure for the detection of brain injury severity and progression in CA victims.

C. Adaptive Markov Process Amplitude

Signal modeling is also used to analyze the EEG in order to predict the future neurological outcome. Bai et al [18] have developed a first order Markov process amplitude (MPA) expressed by the sinusoidal waves to model the EEG signal. The MPA EEG model is applicable to stationary EEG signals. We modified the MPA model where the model parameters are determined adaptively using the LMS algorithm [19]. The model should free us from stationarity constraints and manual calculation of MPA model parameters.

The estimated EEG output $y(n)$ is composed of *K* different oscillations,

$$y(n) = \sum_{j=1}^{K} a_j(n)\sin(2\pi m_j n + \phi_j) \quad (4)$$

where, $a_j(n)$ is the model amplitude of the first order Markov process, m_j is the dominant j^{th} frequency, ϕ_j is the initial phase which was assumed to be equal to zero and *n* is the time index. The next estimate of the model amplitude $a_j(n+1)$ is defined as:

$$a_j(n+1) = \gamma_j(n)a_j(n) + \mu_j(n)\xi_j(n) \quad j = 1,2,...K \quad (5)$$

where,

$\xi_j(n)$ is the independent increment of Gaussian distribution with zero mean and unity variance. μ_j is the coefficient of the random process and γ_j is the coefficient of the first order Markov process ($0 < \gamma_j < 1$).

To adaptively adjust γ and μ, the LMS algorithm introduced by Widrow is used:

$$\gamma_j(n+1) = \gamma_j(n) + \eta_\gamma\left[a_j(n-1)x_j(n)e(n)\right] \quad (6)$$

and

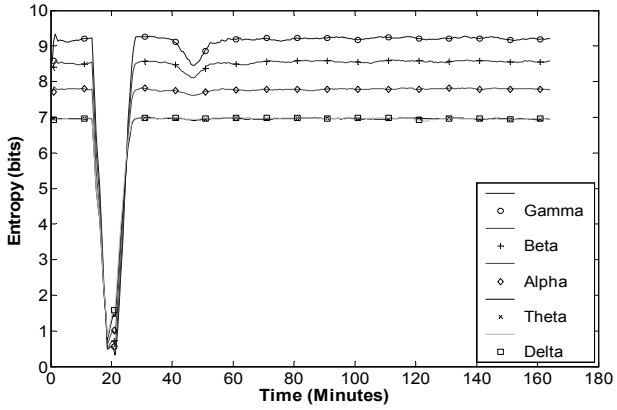
$$\mu_j(n+1) = \mu_j(n) + \eta_\mu\left[\xi_j(n-1)x_j(n)e(n)\right] \quad (7)$$

where η_μ is a small positive constant called the adaptive learning rate which controls the speed of the adjustment [19]. To guarantee model convergence, it can be shown that η_μ should satisfy the condition:

$$0 < \eta_\mu < \frac{1}{\lambda_{\max}} \quad (8)$$

III. RESULTS

The SWE and its time difference were computed for a cohort of rodents. The recovery in different bands is judged by comparing the closeness between $\dot{H}^j(i)$ and zero throughout the different phases of recovery. Fig. 3a, and b shows $H^j(i)$ and $\left|\dot{H}^j(i)\right|$ respectively for an EEG signal obtained from a rodent that was subjected to 3 minutes of asphyxic cardiac arrest. The Entropy is relatively large during the BL period ranging between 7 for Delta and just over 9 bits for Gamma while it drops to below 1 during injury and SP. Immediately after injury, we observe a very fast recovery which is expected from 3 minutes asphyxia. The neurological deficit scoring assessed for this animal after 6 and 24 hours indicated a good outcome.



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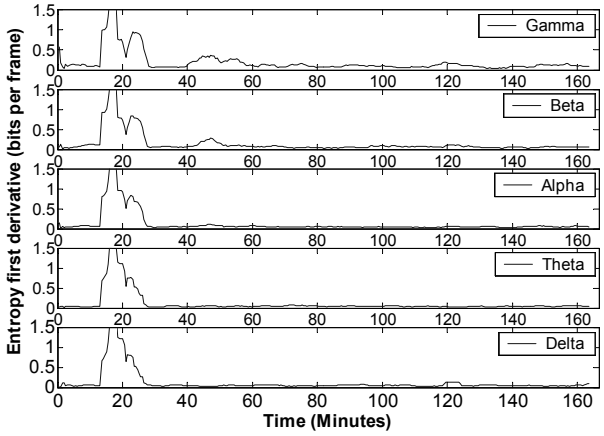


(b)

Fig. 3: (a) The SWE and its (b) first derivative for EEG signals obtained from a rodent that was subjected to 3 minutes asphyxic cardiac arrest.

Fig. 4 a and b shows $H^j(i)$ and $\left|\dot{H}^j(i)\right|$ respectively for an EEG signal obtained from a rodent that was subjected to 7 minutes of asphyxic cardiac arrest. The spiky activity in the

EEG signal is reflected on the SWE. The ER recovery period starts with a rather slow increase in entropy unlike the earlier 3 minutes case. In fact, the entropy of the Gamma band continues to be of a relatively low value that is even lower than the Delta band after 100 minutes from the onset of the ER period. The $\left|\dot{H}^j(i)\right|$ gives more details about these variations. It shows that the entropy rate is low during the ER period. The change and increase in entropy continued for more than 100 minutes after the onset of the ER. The low values of $\left|\dot{H}^j(i)\right|$ might be used as an indicator and a predictor of the final neurological outcome. This obvious lack of recovery indicated a bad neurological outcome. The neurological deficit scoring performed at 6 and 24 Hrs indeed signaled a bad outcome.

The shaded areas of Fig. 5 show the PSD of the normalized EEG signals recorded from one rodent representing the 5 minutes asphyxia during the (a) BL, and (b) ER segments respectively. The PSD of the modeled EEG signal is represented by the dark line envelope. The striking similarities between the original and the modeled signals reflect the capability of the Markov model to simulate EEG signals under different conditions. To quantify the similarity between the actual and modeled EEG signals, the mean square error (MSE) between their power spectral densities was calculated. The Percent normalized MSE was then calculated using:

$$NMSE = \frac{MSE}{Mean\ Signal\ Power} \times 100\% \qquad (9)$$

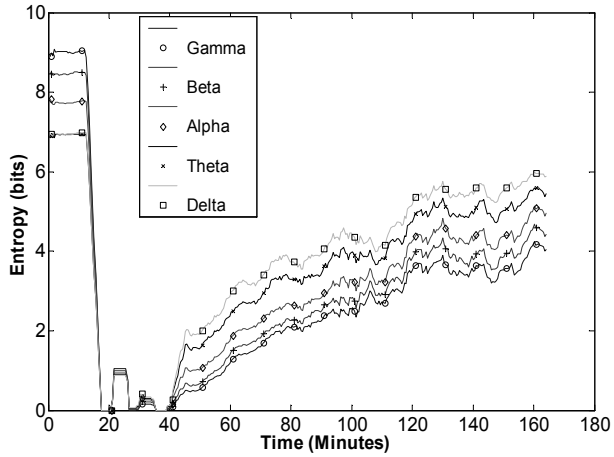
The NMSE was found to be 12%, and 10% for BL and ER segments respectively. Further analysis of the model showed that the second derivative of γ, $\ddot{\gamma}$ amplified the spiking and bursting activity of the EEG signals relative to the background

IV. CONCLUSIONS

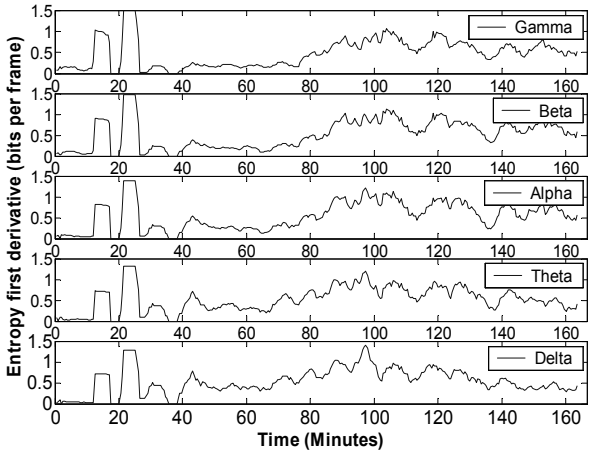
The EEG is a useful tool in clinical neurophysiology and can be used for the identification of cerebral injury. Following global cerebral ischemia by hypoxic-ischemic cardiac arrest, an important observation related to the process of neurological recovery is the presence of spikes and bursts pattern manifested in the EEG. To study the different statistical distributions associated with spiking and random background activity of EEG rhythms, we use quantitative measures related to the amount of "information" content of the signal. Subband Wavelet Entropy (SWE) is used to characterize the interactions between the bursting and random background of EEG rhythms. The wavelet transform is useful for progressively and systematically 'decomposing' the EEG into multi-scaled components.

The EEG is measured from rodent brains in a controlled experimental brain injury model by hypoxic-ischemic cardiac arrest. Results show that while the relative EEG power fails to reveal the order of bursting activity associated with recovery, wavelet entropy is used to segment the EEG and delineate the initial bursting periods in each subband.

Markov process amplitude algorithm is also used to model the EEG signal to identify pathophysiological EEG changes. The EEG signal from the injured brain during various phases of injury and recovery is modeled. Results show that the model is accurate in simulating EEG signal variations following brain injury. The dynamics of the model coefficients successfully capture the presence of spiking and bursting in EEG. Analysis of the Markov model coefficients indicated that the frequency contents of their second derivative amplified the presence of spike and bursts in the EEG. Still however, he optimal choice of the adaptive learning rates and the cross coupling between dominant frequencies seen in the model are areas that need further investigation.

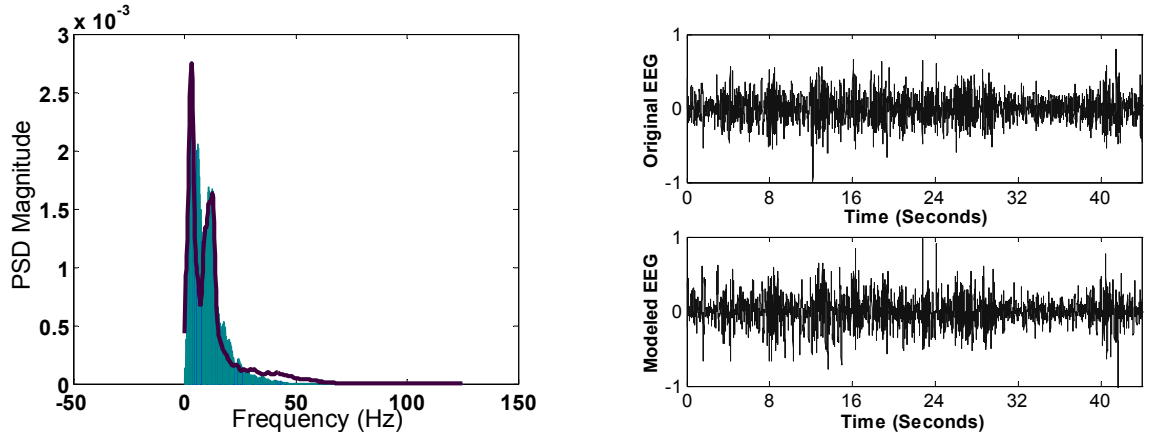


(a)



(b)

Fig. 4: (a) The SWE and (b) the first derivative of the SWE for EEG signals obtained from a rodent that was subjected to 7 minutes asphyxic cardiac arrest.



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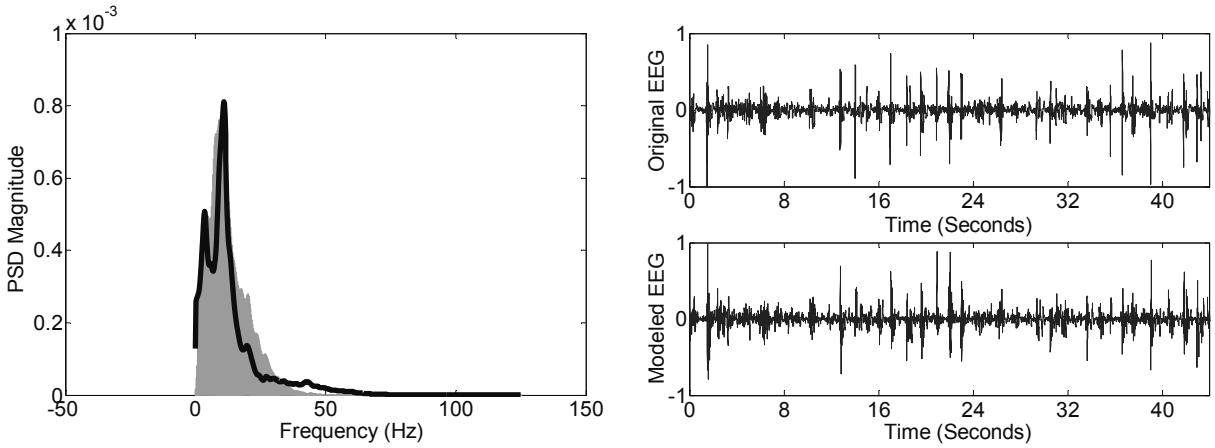

(b)

Fig. 4: Normalized original and modeled EEG signals for the (a) BL, and ER segments.

ACKNOWLEDGMENT

This work represents a very successful collaborative effort between the American University of Sharjah and Johns Hopkins School of Medicine. The author would like to acknowledge and thank the following people: Dr. Nitish Thakor, Joseph Paul, Wendy Ziai, Daniel F. Hanley, and Yousef Al-Assaf. I would also like to thank Amit Malhotra for providing the experimental support.

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